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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,571	DRAPEAU ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31 and 49-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31 and 49-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/11/2006 has been entered.

The amendments to the claims filed on 09/11/2006 have been acknowledged.

Claims 1-31 and 49-64 are pending and currently under examination. Claims 32-48 are cancelled.

NEW MATTER REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-31 and 49-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 49 introduce a new matter by stating that a collagen protein, "said collagen protein from a source other than the demineralized bone matrix;" This phrase constitutes a new matter because nowhere in the specification Applicant stated that the only collagen used in the composition must be only from the source other than demineralized bone matrix. Also, examiner would like to point out that Applicant disclosed on page 8 of the specification, lines 17-23, that a collagen can be from any source.

Claim 58 introduces a new matter by claiming "a sterile" osteoinductive composition. The original claims or the specification do not contain such a phrase and thus this constitutes a new matter. In the presence of the evidence to the contrary, examiner requires that Applicant points out exact place in the specification where such a phrase is presented.

Also, in claim 58, the phrase "an aqueous" diluent constitutes a new matter since Applicant did not specifically point out where such a phrase is present in the specification. In the presence of the evidence to the contrary, examiner requires that Applicant points out exact place in the specification where such a phrase is presented.

Also, in claim 58, the phrase "said collagen solids from a source other than said DBM" constitutes a new matter, since nowhere in the specification such a phrase exists. In the presence of the evidence to the contrary, examiner requires that Applicant points out exact place in the specification where such a phrase is presented.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claims 1 and 64, the Applicant refers to "plasticizer" as part often composition. However, only page 6, line 22 of the specification, mentions that plasticizers can also be added to the osteoinductive composition. The specification does not provide adequate description or examples of plastizers or the weight percent of the plasticizer in comparison to the whole composition; where according to a dictionary a plasticizer is a compound, which increases flexibility and toughness when added to another compound. Further, there are many kinds of plasticizers, for example glycerol or sorbitol, but no examples are provided in the specification.

Applicant responded that the term "plasticizer" is well known in the art.

Examiner disagrees and states that examples of plasticizers, for example, should be placed in the claim, since the claim is overly broad.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 58, the Applicant refers to a "diluent" as part of the composition, however diluent could be any liquid or solid material used to dilute or carry an active ingredient, thus an example of a diluent used in the composition should be provided.

Applicant responded that the claim is amended to "an aqueous diluent" and thus the rejection should be withdrawn.

Examiner disagrees and states that an example of a diluent or an aqueous diluent should be specifically provided.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17, 19-23, 26-28, 31, 49-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. (US 2002/0107570 A1) in view of Boyce et al. (U.S. 2001/0043940 A1).

Sybert et al. teach the use of demineralized bone for repair of spinal disorders. At [0051] Sybert et al. state that the mechanical strength of demineralized bone (herein after referred to as DBM) can be increased by forming chemical linkages between adjacent bone particles by exposing collagen on adjacent bone particles and forming collagen-collagen bonds. At [0042] Sybert et al. state that acid is used to demineralize bone. Sybert et al. state that chemical crosslinkages can be made using irradiation including photooxidation, UV light, microwave, and the like [0052, 0058], dehydrothermal treatment [0052, 0059], enzymatic treatment [0052] including the use of transaminase [0057], glutaraldehyde [0054], formaldehyde [0054], and dicyclohexyl carbodiimide and its derivatives [0054], polyethylene glycol dicycidal ethers [0054], and epsilon amino lysines [0053].

Boyce et al. (U.S. 2001/0043940 A1) state that the bone particles can be combined with one or more biocompatible components, such as plasticizers [0054]; where suitable plasticizers include liquid polyhydroxy compounds as glycerol, or monoacetin etc. See [0060]. (Claim 1)

It would have been obvious to a person having ordinary skill in the art to make a composition comprising crosslinked DBM and collagen because Sybert et al. state that the mechanical strength of DBM can be increased by forming chemical linkages between adjacent bone particles by exposing collagen on adjacent bone particles and forming collagen-collagen bonds, and further to improve the composition by including plasticizers as suggested by Boyce et al. (U.S. 2001/0043940 A1).

It would have been obvious to use carbodiimde (Claims 2, 49) derivatives such as N-(3-dimethylaminopropyl) N-ethylcarbodiimide hydrochloride (Claim 3) and N-hydroxysuccinimide (Claim 4) to perform the crosslinking because Sybert et al. states that carbodiimide derivatives are useful for crosslinking collagens.

It would have been obvious to use glutaraldehyde, formaldehyde/formalin, and, polyethylene glycol dicycidal ethers such as 1,4-butanedoil diglycidyl ether (Claim 13) to perform the crosslinking because Sybert et al. states that these agents are useful for crosslinking collagens.

It would have been obvious to use irradiation including photooxidation, UV light, microwave, and the like (Claims 14, 15, 21, and 22) to perform the crosslinking because Sybert et al. states that these agents are useful for crosslinking collagens.

It would have been obvious to use an enzymatic treatment (Claim 16) such as the use of transaminase (Claim 17) to perform the crosslinking because Sybert et al. states that these agents are useful for crosslinking collagens.

It would have been obvious to use dehydrothermal treatment (Claim 19) to perform the crosslinking because Sybert et al. states that this method is useful for crosslinking collagens.

It would have been obvious to use epsilon amino lysines such as epsilon (gamma glutamyl) lysine (Claim 31) to perform the crosslinking because Sybert et al. states that these agents are useful for crosslinking collagens.

It would have been obvious that all crosslinking reactions would be performed under acidic conditions because Sybert et al. teach that acid is used to demineralize bone (Claim 20).

To accelerate new bone growth and bone healing, Sybert et al. state that growth factors and cementum attachment extracts can be incorporated in, or associated with the DBM [0060, 0062]. Therefore, it would have been obvious to a person having ordinary skill in the art to make a composition comprising crosslinked DBM and collagen and growth factors and cell attachment fragments (Claim 5, 26, 50) because Sybert et al. state that the addition of growth factors will accelerate new bone growth and bone healing. These growth factors and cell attachment fragments may or may not be attached to DBM (Claims 27, 28).

To facilitate bone growth, Sybert et al. state that various types of anterior supporting structures have been employed in intervertebral spinal fusion, i.e. spacers [0082]. Therefore, it would have been obvious to a person having ordinary skill in the art to make a composition comprising crosslinked DBM and collagen and spacers (Claim 23) because Sybert et al. state that the addition of spacer will facilitate bone growth and regeneration.

Claim 53 is included in this rejection because Boyce et al. (U.S. 2001/0043940 A1) teach a composition that is compressed in a mold, where the walls of the mold can be coated with a slurry or a paste containing partially and/or fully demineralized and/or superficially demineralized bone particles to form an osteoimplant. See [0050].

Therefore, it would have been obvious to design a composition of Sybert et al. in a paste form that is used as a material in bone or tissue repair as suggested by Boyce et al. (Claim 53)

Claims 6, 7, 51, and 52 are being included in this rejection because Sybert et al. state at DBM is less than 1 to at least 90 weight % at [0040].

Claims 8, 9, 10, 11, 12, and 53-57 are being included in this rejection because the DBM comprises collagen and is therefore dispersed in collagen. Collagen is a scaffold protein, and the particle size of DBM is an inherent property produced by the method.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. in view of Boyce et al. (U.S. 2002/0107570) as applied to Claims 1 and 16 above, and further in view of Simpson et al. (US 2002/0090725 A1).

The teachings of Sybert et al. are discussed above. Sybert et al. do not teach to crosslink DBM and collagen using lysyl oxidase.

Simpson et al. teach that collagens are routinely crosslinked with lysyl oxidase [0185].

Therefore, it would have been obvious for a person of ordinary skill in the art to crosslink the DBM and collagen of Sybert et al. using the lysyl oxidase of Simpson et al. because Simpson et al. teach that it is routine to cross link collagens with lysyl oxidase and Sybert et al. teach that it is beneficial to expose collagens in DBM and crosslink them to increase the mechanical strength of DBM.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. in view of Boyce et al. (U.S. 2002/0107570) as applied to Claim 1 above, and further in view of Fang et al. (US 5,869,527).

The teachings of Sybert et al. are discussed above. Sybert et al. do not teach to crosslink DBM and collagen by glycation or glycosylation.

Fang et al. teach that collagens are routinely crosslinked by glycation or glycosylation. Column 1, line 21-23.

Therefore, it would have been obvious for a person of ordinary skill in the art to cross link the DBM and collagen of Sybert et al. by glycation or glycosylation of Fang et al. because Fang et al. teach that it is routine to cross link collagens by glycation or glycosylation and Sybert et al. teach that it is beneficial to expose collagens in DBM and crosslink them to increase the mechanical strength of DBM.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. in view of Boyce et al. (U.S. 2002/0107570) as applied to Claim 1 above, and further in view of Bucala et al. (US 5,811,401).

The teachings of Sybert et al. are discussed above. Sybert et al. do not teach the DBM and collagen composition wherein the crosslinks are pentosidine crosslinks.

Bucala et al. teach that fluorescent crosslink pentosidine was isolated from human dura collagen, and that intramolecular pentosidine crosslinking can decrease

solubility of structural proteins such as collagen, and trap serum proteins, such as lipoproteins to structural proteins such as collagen. See column 6, line 37-44.

Therefore, it would have been obvious for a person of ordinary skill in the art to cross link the DBM and collagen of Sybert et al. via intramolecular pentosidine crosslinks of Bucala et al. because Bucala et al. teach that intramolecular pentosidine crosslinking can decrease solubility of structural proteins such as collagen and Sybert et al. teach that it is beneficial to expose collagens in DBM and crosslink them to increase the mechanical strength of DBM.

Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. in view of Boyce et al. (U.S. 2002/0107570)as applied to Claim 1 above, and further in view of Chilkoti et al. (US 6,444,254).

The teachings of Sybert et al. are discussed above. Sybert et al. do not teach polyoxyalkyleneamine spacer or polyethylene glycol spacer in a composition of DBM and collagen.

Chilkoti et al. teach that different kinds of spacers, for example polyethylene glycol spacer that can be used in different compositions as an attachment to ligands or other structures. See column 7, line 38.

Therefore, it would have been obvious for a person of ordinary skill in the to use spacers in a composition of DBM and collagen of Sybert et al., and particularly polyethylene glycol spacer of Chilkoti et al. because Chilcoti et al. teach that it is routine to use spacers such as polyethylene glycol in different compositions.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. in view of Boyce et al. (U.S. 2002/0107570) as applied to Claim 1 above, and further in view of Boyce et al. (US 6,294,041).

The teachings of Sybert et al. are discussed above. Sybert et al. do not teach nonbioabsorbable material, such as methyl methacrylate, in a composition with DBM and collagen.

Boyce et al. teach osteoimplant composed of DBM, collagen, and methyl methacrylate as a reinforcing component in osteoimplant. Column 4, line 35.

Therefore, it would have been obvious for a person of ordinary skill in the art to make a composition of DBM and collagen of Sybert et al. with methyl methacrylate of Boyce et al. because Boyce et al. teach that it is routine to use methyl methacrylate to enforce the structure of the bone implant, composed of DBM and collagen.

Claims 58-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sybert et al. in view of Boyce et al. (U.S. 2001/0043940 A1) and taking further in view of McKay (U.S. 6,261,586 B1).

The teachings of Sybert et al. are disclosed above. Sybert et al. do not teach a plasticizer, or a composition in a paste form, or sterilization via e-beam or gamma irradiation.

Boyce et al. (U.S. 2001/0043940 A1) teach osteoimplant composed of demineralized bone particles, collagen, plasticizers, and also teach how to prepare a

composition having the consistency of a paste. [0067]. The reference does not teach sterilization by gamma or e-beam irradiation.

McKay (U.S. 6,261,586 B1) teaches a bone graft substitute, were its sterilization can be provided by e-bean or gamma irradiation.

To accelerate new bone growth and bone healing, Sybert et al. state that growth factors can be incorporated in, or associated with the DBM [0060, 0062]. Therefore, it would have been obvious to a person having ordinary skill in the art to make a composition comprising crosslinked DBM and collagen and growth factors (Claim 59) because Sybert et al. state that the addition of growth factors will accelerate new bone growth and bone healing. These growth factors and cell attachment fragments may or may not be attached to DBM (Claims 27, 28).

Claims 62 is being included in this rejection because Sybert et al. state at DBM is less than 1 to at least 90 weight % at [0040].

Claim 63 is being included in this rejection because the DBM comprises collagen and is therefore dispersed in collagen. Collagen is a scaffold protein, and the particle size of DBM is an inherent property produced by the method.

Therefore, it would have been obvious to one skilled in the art to design a cross-linked composition comprising of a demineralized matrix, and collagen as described by Sybert at, and to improve on that design by forming a product in a paste form, that

contains plasticizers as taught by Boyce et al., and additionally sterilize the composition using e-beam or gamma irradiation as taught by McKay, where the method is commonly used in the art as a common procedure to sterilize implants before their insertion into a subject.

Applicant's Arguments regarding 35 U.S.C. 103 (a) Rejection

Applicant states that claims 1 and 49 as amended require that the collagen be from a source other than said demineralized bone matrix, and thus the rejection should be withdrawn.

Examiner disagrees because, in the absence of the evidence to the contrary, collagen from different sources will have the same properties for purposes of the instant invention. Further, Applicant points out and specifically claims on page 8, lines 17-23 of the specification that the collagen of the instant invention can be from any source.and can be of any type.

Further, Applicant states that in each case, the tertiary reference is relied upon as teaching a specific crosslinking agent or material for incorporation in the composition, does not motivate one of skill in the art to make combination of features provided in clams 1 and 49.,

Examiner disagrees because all those agents disclosed by the tertiary references are very well known and commonly used crosslinking agents.

Moreover, Applicant states that Sybert et al. relates to a band structure for repairing spinal disorders, and that both Sybert et al. and Boyce et al. teach end products that are solids and not pastes.

Examiner points out that Boyce et al. teach pastes as an intermediate product, therefore the prior art applies to the rejection.

Moreover, Applicant states that claim 58, as amended, refers to "a sterile osteoinductive composition in a paste form" and that Boyce et al. does not suggest that the paste should be sterilized.

Examiner disagrees and states that sterilization is commonly used where different compositions for tissue repair are used, therefore Boyce et al. would still apply, since it is a common practice in the art to sterilize compositions before applying them to the tissues of interest.

Applicant refers to the remaining rejections very generally, thus examiner will respond also generally, that the secondary or tertiary references positively motivate one of the ordinary skilled in the art to make the combination of features as described and claimed in the instant invention. Therefore, the rejections are maintained.

Conclusion

No claims are allowed.

Since no new art rejections were presented, and new rejections are necessitated by the amendments to the claims **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-273-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

Karen Cochrane Carlson PhD

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PRIMARY EXAMINER